

**REMARKS**

This Amendment responds to the non-final Office Action mailed February 10, 2006. Inasmuch as the Office Action set a three-month shortened statutory period for response, to end May 10, 2006, this response is accompanied by a Request for Two-Month Extension of Time and required fee.

The Office Action rejects claims 1-16. With the present amendment, Applicants cancel claims 6, 7, 9, 10, and 12-15, amend claims 1-3, 5, 8, 11, and 16, and add new claims 17 and 18. Applicants add no new matter with this amendment and support is generally provided throughout the specification. Applicants specifically point out the support for the amendments in responding to particular points hereinafter.

**Priority**

The Office Action fails to acknowledge Applicants' claim of priority under 35 U.S.C. §119. Applicants respectfully request that the Office acknowledge Applicants' claim in the next official communication.

**Information Disclosure Statements**

Applicants note that the Office Action includes an initialed copy of the Form PTO-1449 filed with the Information Disclosure Statement on August 16, 2005. Applicants thank the Examiner for indicating consideration of the listed documents.

**Claim Rejections – 35 U.S.C. § 112, First Paragraph**

The Office Action rejects claims 1-16 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement, for a number of reasons. Rather than detail the rejections, and Applicants' response thereto, Applicants note that the present amendment is responsive to each point raised by the Office Action. However, Applicants note that any amendments made herein are solely for purposes of advancing prosecution, and no acquiescence with or agreement to the Office Action's rejections should be inferred.

With regard to the present amendments, Applicants note that support is provided in at least the following passages of the specification. The amendment to refer to the liposome adsorbing the recombinant plasmid is based on at least the following description: "a cationic liposome capable of adsorbing the recombinant plasmid to the surface thereof." (See lines 22 to 23 of page 22).

The amendment to add the clause, "wherein the porous block body is impregnated with the recombinant plasmid, the basic Fibroblast Growth Factor, and the cationic liposome so that the recombinant plasmid adsorbed to the cationic liposome is carried by the porous block body through the cationic liposome," is based on at least the following descriptions: "The hydroxyapatite porous sintered body was impregnated with these phosphate buffers . . . [and] . . [i]n this way, an osteogenic treatment device was obtained," (see lines 3 to 7 of page 27), and "in a case where a liposome is used as a vector . . . a recombinant plasmid (nucleic acid) adsorbed to or incorporated in the liposome is also carried

by the base body stably for a long time" (see line 18 of page 37 to line 1 of page 38).

Applicants note that the Office Action states that the specification fails to describe porous base bodies having communicating holes. In response to this particular point, Applicants note that the specification discloses the manufacturing process of the base body (porous block body) in line 4 of page 38 to line 17 of page 39, line 8 of page 43 to line 12 of page 44, lines 17 to 22 of page 45, and lines 1 to 7 of page 46. The specification further states that "[i]n such a porous block body, each hole is not a closed hole separated from adjacent holes" (see lines 7 to 9 of page 34) and "cells involved in bone formation move (diffuse) in the base body 1 in such a manner that they fill a hole 1a first and then overflow into an adjacent hole 1a" (see lines 22 to 25 of page 35).

In view of the present amendments and remarks, Applicants respectfully submit that the claims are fully enabled by the specification and request withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

### **Claim Rejections – 35 U.S.C. § 112, Second Paragraph**

The Office Action rejects claims 1 and 16 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for the recitation of "base sequence derived from" and "non-viral vector holding the nucleic acid." In response, Applicants respectfully submit that one of skill in the art would immediately understand the metes and bounds of Applicants' claim terminology. However, solely in an effort to advance prosecution, and without acquiescing to or agreeing with the Office

Actions' rejection, Applicants have amended claims 1 and 16 to even more clearly recite the claimed invention. Applicants respectfully request withdrawal of the rejection for indefiniteness.

### **Claim Rejections – 35 U.S.C. § 103**

The Office Action rejects claims 1-8 and 11-16 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over JP2001-505097 (translation of record), JP 2000-302567 (translation of record) and Street et al. (PNAS 99(15):9656-9661, July 2002), ("STREET").

Prior to discussing the rejection in detail, Applicants respectfully note that the claims have been amended and that the amendments obviate the art-based rejections. Applicants note that these amendments are made solely in an effort to advance prosecution, and that no agreement to or acquiescence with, the rejections of record, should be inferred.

Applicants respectfully submit that the art cited by the Office Action does not render obvious the claimed invention.

The Office Action cites JP2001-505097 for its disclosure of "an osteogenic treatment device comprising a DNA encoding a protein of osteogenesis, more specifically a BMP family member and a biodegradable porous matrix containing tricalcium phosphate ceramics with continuous micropores in the volume range of 20-60%." The Office Action states that JP2001-505097 also teaches that the osteogenic treatment device includes mixtures with various kind of osteogenesis.

Applicants note, as also admitted by the Examiner, JP2001-505097 does not teach or suggest the use of an angiogenic factor, such as, for example, basic Fibroblast Growth Factor. Further, although JP2001-505097 also seems to suggest that the DNA is used with an expression vector, the Japanese application does not teach what kind of expression vector can be used. Therefore, JP2001-505097 does not only fail to teach the angiogenic factor in the osteogenic device, but also does not teach or suggest that the DNA is adsorbed on the surface of a non-viral vector, especially a cationic liposome.

The Examiner recites JP2000-302567 as disclosing a "sintered compact that is made of porous calcium phosphate with a porosity of 55 to 90% and spherical pores that communicate with one another." The Examiner refers to the disclosed pore structure with an average diameter of the communicating parts between the pores of not less than 50  $\mu\text{m}$  and pore diameters of not less than 150  $\mu\text{m}$ . The Examiner admits that JP2000-302567 does not teach the application in gene therapy.

In response, Applicants respectfully submit that JP2000-302567 does not teach or suggest that the sintered compact is used with a recombinant plasmid and a non-viral vector, especially a cationic liposome. Thus, JP2000-302567 does not remedy the deficiencies of JP2001-505097, and fails to provide the missing elements of the presently claimed invention.

The Office Action summarizes STREET as teaching "that the angiogenic factors are also osteogenic factors and therefore the two processes of angiogenesis in bone formation and generation of bone itself are inextricably

linked." Applicants note, however, that STREET only teaches the role and the interaction of these factors. Namely, STREET does not teach or suggest that the factors are used with a porous block body as a bone implant (osteogenic treatment device). Moreover STREET does not teach nor suggest that a DNA encoding a protein of osteogenesis (BMP) is used with a non-viral vector, especially a cationic liposome. Therefore, the combination of the teaching of STREET and JP2001-505097 and JP2000-302567 does not result in the presently claimed invention.

Applicants respectfully request withdrawal of the rejections over JP2001-505097, JP2000-302567, and STREET.

The Office Action further rejects claims 1-8 and 11-16 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Application No. 2002/0082694 to McKay ("McKAY"), together with JP2000-302567 and STREET.

The rejection asserts that McKAY "teaches an osteogenic treatment device comprising a DNA encoding a protein of osteogenesis, more specifically a BMP family member and a biodegradable porous matrix containing tricalcium phosphate ceramics or hydroxyapatite dispersed into a collagen slurry. It also teaches a mixture with other proteins that are osteogenic enhancing factors." The Office Action admits that McKAY does not specifically teach an angiogenic factor and the specific dimensions and properties of the instant invention.

Applicants note that McKAY also fails to teach or suggest that the DNA is used with a non-viral vector, especially a cationic liposome. Therefore, the

combination of the teaching of McKAY, STREET, and JP2000-302567 does not result in all of the features of the presently claimed invention. Given the lack of all the claimed features, Applicants respectfully submit that there is no reasonable expectation of success in the combination. Still further, there is no reason to modify any of the teachings to arrive at the presently claimed invention.

In view of the foregoing amendments and remarks, Applicants respectfully request withdrawal of the obviousness rejection of claims 1-8 and 11-16 under 35 U.S.C. § 103(a).

## CONCLUSION

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the rejections of record and allow the pending claims. Allowance of the application is requested, with an early mailing of the Notice of Allowance and Allowability.

Respectfully Submitted,  
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